AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions and listings of the claims.

1. (Currently Amended) A ~~human~~ recombinant human lysosomal enzyme or variant thereof produced in END3 complementation group CHO cells, ~~or a derivative of said enzyme or variant,~~ wherein said ~~enzyme has a high level of phosphorylation and a low level of unphosphorylated high-mannose oligosaccharides~~ END3 complementation group CHO cell is a G71 cell line or derivative thereof, wherein said enzyme is secreted from said G71 cell line or derivative thereof in amounts of at least 1 picogram/cell/day, and wherein at least 70% of said secreted enzyme binds to the cation-independent mannose-6-phosphate receptor (CI-M6PR).

2. (Original) The enzyme of claim 1, wherein said enzyme is selected from the group consisting of: acid alpha glucosidase, aspartylglucosaminidase, acid lipase, cysteine transporter, Lamp-2, α-galactosidase A, acid ceramidase, α-L-fucosidase, β-hexosaminidase A, GM2-activator deficiency, α-D-mannosidase, β-D-mannosidase, arylsulfatase A, saposin B, neuraminidase, α-N-acetylglucosaminidase phosphotransferase, phosphotransferase γ-subunit, L-iduronidase, iduronate-2-sulfatase, heparan-N-sulfatase, α-N-acetylglucosaminidase, acetylCoA:N-acetyltransferase, N-acetylglucosamine 6-sulfatase, galactose 6-sulfatase, β-galactosidase , N-acetylgalactosamine 4-sulfatase, hyaluronoglucosaminidase, multiple sulfatases, palmitoyl protein thioesterase, tripeptidyl peptidase I, acid sphingomyelinase, cholesterol trafficking, cathepsin K, α-galactosidase B, and sialic acid transporter.

3. (Currently Amended) The enzyme of claim 2, wherein said enzyme is ~~A human recombinant~~ acid alpha glucosidase (rhGAA)~~, or variant thereof produced by END3 complementation group CHO cells, or a derivative of said enzyme or variant, wherein said rhGAA has a high level of phosphorylation and low level of unphosphorylated high-mannose oligosaccharides~~.

4. (Canceled)

5. (Currently Amended) A method for producing ~~highly phosphorylated human~~ a recombinant human lysosomal enzyme~~s~~ or variant~~s~~ thereof, comprising the steps of:

(a) culturing Chinese Hamster Ovary (CHO)-derived END3 complementation group cells;

(b) ~~preparation of~~ preparing a mammalian expression vector suitable for said END3 complementation group cells;

(c) ~~transfection of~~ transfecting said END3 complementation group cells with said expression vector;

(d) ~~selection~~ selecting and cloning of a END3 complementation group transfectant; and

(e) ~~optimization of~~ optimizing cell culture process methods for manufacturing said enzyme,

wherein said CHO-derived END3 complementation group cell is a G71 cell line or derivative thereof,

wherein said enzyme is secreted from said G71 cell line in amounts of at least 1 picogram/cell/day, and

wherein at least 70% of said secreted enzyme binds to the cation-independent mannose-6-phosphate receptor (CI-M6PR).

6. (Currently Amended) The method of claim 5, wherein said enzymes ~~have a low level of unphosphorylated high mannose oligosaccharides~~ is acid alpha glucosidase (rhGAA).

7. (Currently Amended) A composition comprising the recombinant human lysosomal enzyme~~,~~ or variant ~~or derivative~~ thereof produced by the method of claim 5.

8. (Currently Amended) A pharmaceutical composition comprising the recombinant human lysosomal enzyme~~,~~ or variant thereof ~~or derivative~~ of claim 7 and a pharmaceutically acceptable carrier, diluent or excipient.

9. (Canceled)

10. (Currently Amended) A method for producing ~~highly phosphorylated human~~ recombinant human acid alpha glucosidase ~~(hrGAA)~~ (rhGAA) or variant thereof, comprising the steps of:

(a) culturing Chinese Hamster Ovary (CHO)-derived END3 complementation group cells;

(b) ~~preparation of~~ preparing a mammalian expression vector suitable for said END3 complementation group cells;

(c) ~~transfection of~~ transfecting said END3 complementation group cells with said expression vector;

(d) ~~selection~~ selecting and cloning of a END3 complementation group transfectant; and

(e) ~~optimization of~~ optimizing cell culture process methods for manufacturing said rhGAA, wherein said CHO-derived END3 complementation group cell is a G71 cell line or derivative thereof,

wherein said rhGAA is secreted from said G71 cell line in amounts of at least 1 picogram/cell/day, and

wherein at least 70% of said secreted enzyme binds to the cation-independent mannose-6-phosphate receptor (CI-M6PR).

11. (Canceled)

12. (Currently Amended) A ~~highly phosphorylated~~ composition comprising ~~recombinant acid alpha glucosidase (hrGAA)~~rhGAA~~,~~ or variant ~~or derivative~~ thereof, produced by the method of claim 10.

13. (Currently Amended) A pharmaceutical composition comprising the ~~recombinant acid alpha glucosidase, (hrGAA)~~rhGAA, or variant ~~or derivative~~ thereof, of claim 12 and a pharmaceutically acceptable carrier, diluent or excipient.

14. (Canceled)

15. (Currently Amended) A method of treating a deficiency of a lysosomal enzyme comprising administering to a subject in need of said lysosomal enzyme~~,~~ a therapeutically effective amount of said lysosomal enzyme, wherein said lysosomal enzyme to be administered is a ~~human~~ recombinant human lysosomal enzyme~~,~~ or variant thereof produced by CHO-derived END3 complementation group cells, ~~or a derivative of said enzyme or variant~~wherein said CHO-derived END3 complementation group cell is a G71 cell line or derivative thereof, wherein said enzyme is secreted from said G71 cell line in amounts of at least 1 picogram/cell/day, and wherein at least 70% of said secreted enzyme binds to the cation-independent mannose-6-phosphate receptor (CI-M6PR).

16. (Currently Amended) The method of claim 15, wherein said lysosomal enzyme deficiency is selected from the group consisting of: aspartylglucosaminuria, cholesterol ester storage disease, Wolman disease, cystinosis, Danon disease, Fabry disease, Farber lipogranulomatosis, Farber disease, fucosidosis, galactosialidosis types I/II, Gaucher disease types I/II/III, Gaucher disease, globoid cell leukodystrophy, Krabbe disease, glycogen storage disease II, Pompe disease, GM1-gangliosidosis types I/II/III, GM2-gangliosidosis type I, Tay Sachs disease, GM2-gangliosidosis type II, Sandhoff disease, GM2-gangliosidosis, α-mannosidosis types I/II, β-mannosidosis, metachromatic leukodystrophy, mucolipidosis type I, sialidosis types I/II mucolipidosis types II /III I-cell disease, mucolipidosis type IIIC pseudo-Hurler polydystrophy, mucopolysaccharidosis type I, mucopolysaccharidosis type II, Hunter syndrome, mucopolysaccharidosis type IIIA, Sanfilippo syndrome, mucopolysaccharidosis type IIIB, mucopolysaccharidosis type IIIC, mucopolysaccharidosis type IIID, mucopolysaccharidosis type IVA, Morquio syndrome, ~~of~~ mucopolysaccharidosis type IVB Morquio syndrome, mucopolysaccharidosis type VI, mucopolysaccharidosis type VII, Sly syndrome, mucopolysaccharidosis type IX, multiple sulfatase deficiency, neuronal ceroid lipofuscinosis, CLN1 Batten disease, CLN2 Batten disease, Niemann-Pick disease types A/B, Niemann-Pick disease, Niemann-Pick disease type C1, Niemann-Pick disease type C2, pycnodysostosis, Schindler disease types I/II, Schindler disease, and sialic acid storage disease.

17. (Canceled)

18. (New) The method of claim 16, wherein said lysosomal deficiency is Pompe disease.

19. (New) The method of claim 18, wherein said recombinant human lysosomal enzyme is acid alpha glucosidase (rhGAA).

20. (New) The enzyme of claim 2, wherein said enzyme is tripeptidyl peptidase I (TPP I).

21. (New) The method of claim 5, wherein said enzyme is TPP I.

22. (New) The composition of claim 7, wherein said enzyme is TPP I.

23. (New) The pharmaceutical composition of claim 8, wherein said enzyme is TPP I.

24. (New) The method of claim 16, wherein said lysosomal deficiency is CLN2 Batten disease.

25. (New) The method of claim 24, wherein said recombinant human lysosomal enzyme is TPP I.

26. (New) A recombinant human galactose 6-sulfatase (rhG6S) or variant thereof produced in END3 complementation group CHO cells, wherein said END3 complementation group CHO cell is a G71 cell line or derivative thereof, and wherein said rhG6S is secreted from said G71 cell line in amounts of at least 1 picogram/cell/day.

27. (New) A method for producing recombinant human galactose 6-sulfatase (rhG6S) or variant thereof, comprising the steps of:

(a) culturing Chinese Hamster Ovary (CHO)-derived END3 complementation group cells;

(b) preparing a mammalian expression vector suitable for said END3 complementation group cells;

(c) transfecting said END3 complementation group cells with said expression vector;

(d) selecting and cloning of a END3 complementation group transfectant; and

(e) optimizing cell culture process methods for manufacturing said rhG6S, wherein said CHO-derived END3 complementation group cell is a G71 cell line or derivative thereof, and

wherein said rhG6S is secreted from said G71 cell line in amounts of at least 1 picogram/cell/day.

28. (New) A composition comprising rhG6S, or variant or derivative thereof, produced by the method of claim 27.

29. (New) A pharmaceutical composition comprising the rhG6S, or variant or derivative thereof, of claim 28 and a pharmaceutically acceptable carrier, diluent or excipient.

30. (New) A method of treating a deficiency of a lysosomal enzyme comprising administering to a subject in need of said lysosomal enzyme a therapeutically effective amount of said lysosomal enzyme, wherein said deficiency is Mucopolysaccharidosis type IVA (Morquio syndrome) and said lysosomal enzyme to be administered is a recombinant

human galactose-6-sulfatase (rhG6S) or variant thereof produced by CHO-derived END3 complementation group cells, wherein said CHO-derived END3 complementation group cell is a G71 cell line or derivative thereof, and wherein said rhG6S is secreted from said G71 cell line in amounts of at least 1 picogram/cell/day.